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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants	:	Hans Carlsson et al.
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Filed	:	May 19, 1999
For	:	VACCINE DELIVERY SYSTEM AND METHOD OF PRODUCTION
Examiner	:	V. Portner
Group Art Unit	:	1645

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I hereby certify that this paper is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Assistant Commissioner for Patents Washington, D.C. 20231 on October 2, 2002.

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AMENDMENT AND RESPONSE

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Box AF
Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

This communication is in response to the final Office Action mailed April 4, 2002. Reconsideration is respectfully requested in view of the following amendments and remarks.

stabilizing agents added prior to mixing to stabilize the W/O emulsion in the presence of the solubilizing agent(s) and promote the incorporation of the water insoluble protein within the polymer particles during step (b); and

(b) forming droplets of said W/O emulsion by dispersing the emulsion in a fluid medium, and removing said solvent from the O phase of the W/O emulsion droplets to thereby form the polymer particles incorporating the water insoluble protein antigen.

D1

16. (Twice Amended) The method of claim 12, wherein the hydrophilic surfactant is a zwitterionic surfactant selected from the group consisting of 3-1-propanesulphonate (CHAPS), 3-[(3-cholamidopropy1)-dimethylammonio]-2-hydroxy-1-propanesulphonate (CHAPSO), N,N-*bis*-cholamide (BIGCHAP), N,N-bis-deoxycholamide (deoxy BIGCHAP), lyso phosphatidylcholine, alkylbetaines and sulphobetaines.

D2

18. (Twice Amended) The method of claim 17, wherein the one or more chaotropic agents is/are selected from the group consisting of a perchlorate, thiocyanate, guanidine, chlorate, iodide, bromide, nitrate and urea.

D3

19. (Twice Amended) The method of claim 1 which includes a Double Emulsion (W/O/X) Solvent Evaporation Technique wherein the fluid medium in which the stabilized W/O emulsion is dispersed in step (b) is a liquid phase (X) which is immiscible with the O phase, said method producing a W/O/X

double emulsion comprising W/O droplets from which the solvent is evaporated.

20. (Twice Amended) The method of claim 1 which includes a Double Emulsion (W/O/X) Solvent Extraction Technique wherein the fluid medium in which the stabilized W/O emulsion is dispersed in step (b) is a liquid phase (X) which is immiscible with the O phase, said method producing a W/O/X double emulsion comprising W/O droplets, and wherein the removal of the organic solvent from the O phase of the droplets is achieved through extraction by the X phase.

D3

23. (Twice Amended) The method of claim 1, wherein the dispersal of the stabilized W/O emulsion in a fluid medium during polymer formulation in step (b) is achieved with a spray drying technique, wherein the stabilized W/O emulsion is dispersed in a gaseous medium to form a spray of W/O emulsion droplets from which said solvent evaporates.

D4

24. (Twice Amended) The method of claim 1, wherein the dispersal of the stabilized W/O emulsion in a fluid medium during polymer particle formulation in step (b) is achieved with a fluid gas technique.

32. (Twice Amended) The method of claim 1, wherein the matrix polymer is a homo-or co-polymer selected from one or more of the group consisting of polyesters, polyanhydrides, polyorthoesters, polycarbonates, polyamides, poly(amino acids), polyacetals, polycyanoacrylates, polyacrylates,

D5

biodegradable polyurethanes, non-erodible polyurethanes, polymers of ethylene-vinyl acetate, acyl substituted cellulose acetates, polysaccharides, polystyrenes, polyvinyl chloride, polyvinyl fluoride, poly(vinyl imidazole), chlorosulphonated polyolefins, polyethylene oxide, polyethers and polyoxalates.

37. (Twice Amended) A vaccine delivery system produced by the method of claim 1, wherein the one or more stabilizing agents is/are a polymer selected from the group consisting of poly(vinyl pyrrolidone), poly(vinyl alcohol), polysaccharides, polyethyleneoxide and water soluble proteins, and wherein the method includes a Double Emulsion (W/O/X) Solvent Evaporation Technique wherein the fluid medium in which the stabilized W/O emulsion is dispersed in step (b) is a liquid phase (X) which is immiscible with the O phase, said method producing a W/O/X double emulsion comprising W/O droplets from which the solvent is evaporated.

45. (Twice Amended) The vaccine delivery system of claim 37, wherein the matrix polymer is a homo- or co-polymer selected from one or more of the group consisting of polyesters, polyanhydrides, polyorthoesters, polycarbonates, polyamides, poly(amino acids), polyacetals, polycyanoacrylates, polyacrylates, biodegradable polyurethanes, non-erodible polyurethanes, polymers of ethylene-vinyl acetate, acyl substituted cellulose acetates, polysaccharides, polystyrenes, polyvinyl chloride, polyvinyl fluoride, poly(vinyl imidazole),

chlorosulphonated polyolefins, polyethylene oxide, polyethers and polyoxalates.

49. (Twice Amended) The vaccine delivery system of any one of claims 37 and 45-48, wherein the polymer particles have an average diameter of 0.05-20 μm according to the volume size distribution.

50. (Twice Amended) A composition comprising the vaccine delivery system of any one of claims 37 and 45-48.

51. (Twice Amended) A method for the treatment of existing *Helicobacter* infection in a mammalian host, comprising administering to the mammalian host an effective amount of the composition according to claim 50 wherein the water insoluble protein antigen is a *Helicobacter* antigen.

52. (Twice Amended) A method for preventing or reducing the risk of *Helicobacter* infection in a mammalian host, comprising administering to the mammalian host an effective amount of the composition according to claim 50 wherein the water insoluble protein antigen is a *Helicobacter* antigen.

58. (Amended) A composition comprising the vaccine delivery system of claim 49.

59. (Amended) A method for the treatment of existing *Helicobacter* infection in a mammalian host comprising administering to the mammalian host an effective amount of the

composition according to claim 58 wherein the water insoluble protein antigen is a *Helicobacter* antigen.

60. (Amended) A method for preventing or reducing the risk of *Helicobacter* infection in a mammalian host, comprising administering to the mammalian host an effective amount of the composition according to claim 58 wherein the water insoluble protein antigen is a *Helicobacter* antigen.